The Neurohospitalist
1(2) 85-93

DOI: 10.1177/1941875210395775
http://nhos.sagepub.com

Aspiration Pneumonia After Stroke: Intervention and Prevention

John R. Armstrong, MD, FCCP[1], and Benjamin D. Mosher, MD, FACS[1]

Abstract

Fifteen million strokes occur worldwide each year with 5 million associated deaths and an additional 5 million people left permanently disabled. In the United States, about 780 000 people suffer a new or recurrent stroke each year. There were an estimated total 5.8 million stroke survivors as of 2008. Mortality from stroke is the third leading cause of death in America following heart disease and cancer. Chest infection may affect up to as many as one-third of stroke patients. This increases the morbidity and mortality of this patient population. Pneumonia causes the highest attributable mortality of all medical complications following stroke. A comprehensive multidisciplinary team approach is required at the hospital level. This requires active administrative commitment and participation. Implementation of evidence-based management strategies can improve outcomes and reduce costs. We sought to review the problem of post-stroke pneumonia and discuss strategies for prevention and intervention.

Keywords

stroke, pneumonia, aspiration

Introduction

Fifteen million strokes occur worldwide each year with two-thirds involving permanent disability or death.[1] The United States contributes about three-quarter of a million new or recurrent strokes each year. This is associated with an annual cost of $65.5 billion.[1] Stroke is the third leading cause of death in America following heart disease and cancer.[2]

Up to one-third of stroke patients suffer from pneumonia.[3] This increases the morbidity and mortality of this patient population. Pneumonia causes the highest attributable mortality of all medical complications following stroke.[4] Respiratory failure from stroke leads to intubation in up to 6% of patients suffering an ischemic stroke and 30% of patients with a hemorrhagic stroke.[5] The application of ventilator support carries its own independent risk of pneumonia. Pneumonia accounts for an estimated one-third of nosocomial infections in critical care units according to the national nosocomial infection surveillance system. The mortality rate from ventilator-associated pneumonia (VAP, defined as pneumonia developed while on the ventilator) is estimated to be 20% to 30%.[6] The total costs per occurrence is $50 000.[7,8]

These high-risk, high-cost, high-volume events present a major challenge to our society, public health systems, and providers. The purpose of this article is to review the problem of post-stroke pneumonia and discuss evidence-based management strategies for prevention and intervention.

Who Gets Pneumonia After Stroke and Why

There are many different causes of pneumonia. These causes can be grouped into broad categories: community-acquired pneumonia, hospital-acquired pneumonia, health care−associated pneumonia, ventilator-associated pneumonia, aspiration pneumonia, pneumonia caused by opportunistic organisms, and other. Most available data suggests post-stroke pneumonia is often due to aspiration. Ill hospitalized patients routinely aspirate and patients with an impaired swallowing mechanism due to neurological injury are at especially high risk.[9] While the presence of an endotracheal tube may provide some protection against large volume aspiration, the endotracheal tube also interferes with normal defense mechanisms and does not prevent smaller aspiration of pharyngeal or gastric contents.[10,11]

Normal swallowing involves multiple complex and coordinated interactions. These interactions involve both the central and peripheral nervous system. Normal swallowing involves

[1] Michigan State University College of Human Medicine, Lansing, MI, USA

Corresponding Author:
John R. Armstrong, Sparrow Health System, Michigan State University College of Human Medicine, 1200 E Michigan Avenue, Suite 415, Lansing, MI 48912, USA
Email: john.armstrong@sparrow.org

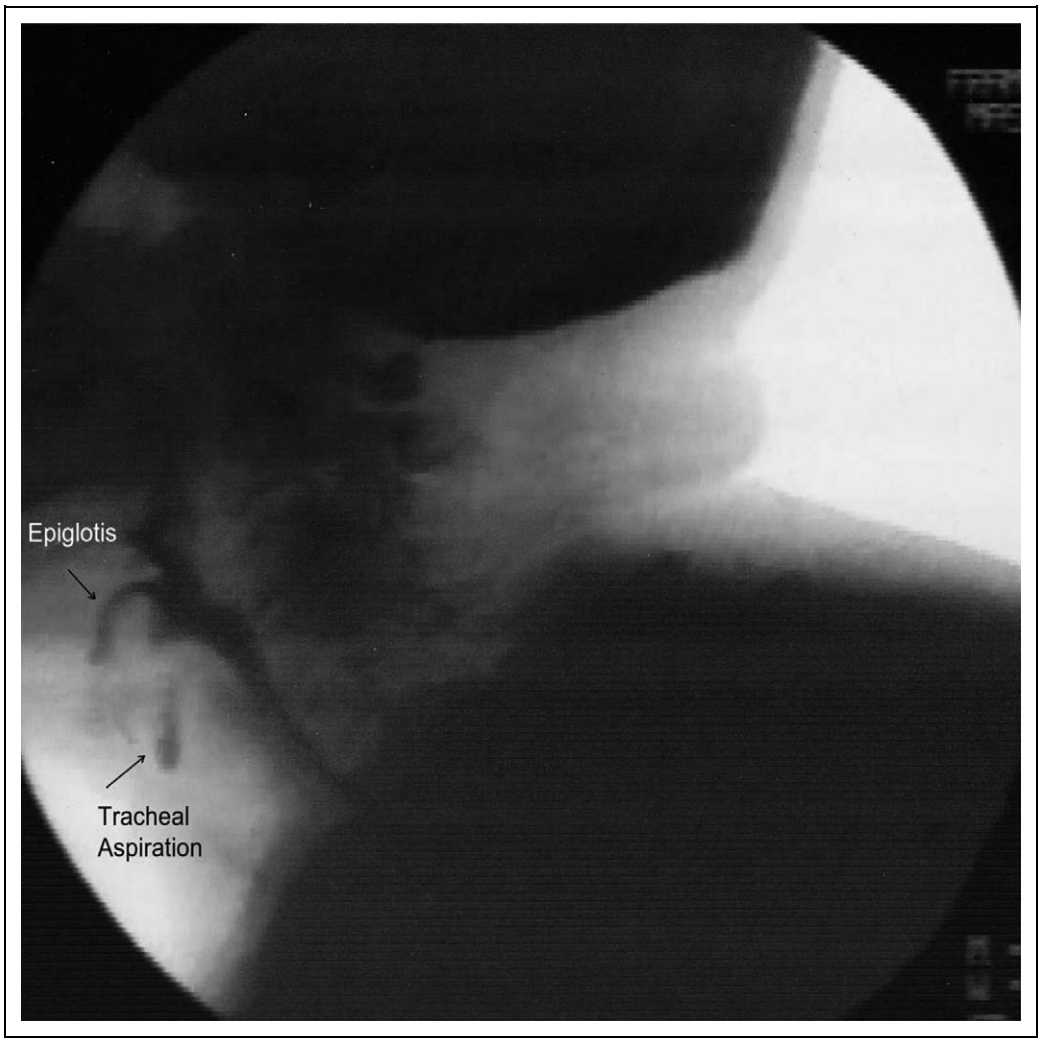

Figure 1. Video swallowing study of 67-year-old male with recent stroke with evidence of aspiration.

4 phases: (1) oral, (2) oral propulsive, (3) pharyngeal, and (4) esophageal. Mastication and preparation make up the oral phase. The oral propulsive phase begins as the soft palate lifts to close the nasopharynx and propel the bolus posteriorly. During the pharyngeal phase, there is upward movement of the hyoid and larynx, closure of the vocal cords, closure of the epiglottis over the airway, and pharyngeal contraction to propel the bolus. The esophageal phase involves propulsion of the bolus along the esophagus to the stomach. The term penetration refers to the leakage of material into the larynx to the level of the true vocal folds (Figure 1). This is a strong indicator of aspiration risk. True aspiration indicates tracheal contamination.[12]

Stellars et al in a prospective study identified several independent risk factors for developing post-stroke pneumonia in the hospital.[3] Ten parameters were assessed in 412 patients as predictors of pneumonia following stroke. Standardized criteria were used to establish the presence of in-hospital chest infection.[13] The findings of this study confirm the multifactorial nature of post-stroke pneumonia. It also identified many predictors of which stroke patients would develop pneumonia. Five of the ten tested parameters were useful predictors: age >65 years, dysarthria or no speech due to aphasia, modified Rankin Scale $\geq$4, abbreviated mental test score <8, and a failed bedside progressive water swallow test. Two or more of these factors correctly predicted pneumonia with 90.9% sensitivity and 75.6% specificity. Interestingly, oral health was not an independent predictor in this study. Other studies have indicated an association of COPD, smoking,[14] level of dependence,[15] oral health status, and presence of bacterial pathogens in the mouth[16] with the development of pneumonia in patients post stroke.

As many as one-half of patients with stroke have a dysfunctional swallow and about one-third aspirate on video swallow.[12,17,18] Among patients that aspirate, one-third develop pneumonia. Half the patients that aspirate do it silently.[18] The location of the stroke does not appear to assist in aspiration risk assessment. McCullough et al noted in a series of 160 patients that bilateral subcortical stroke patients seemed to have an increased occurrence of aspiration over other types of unilateral and bilateral stroke patients.

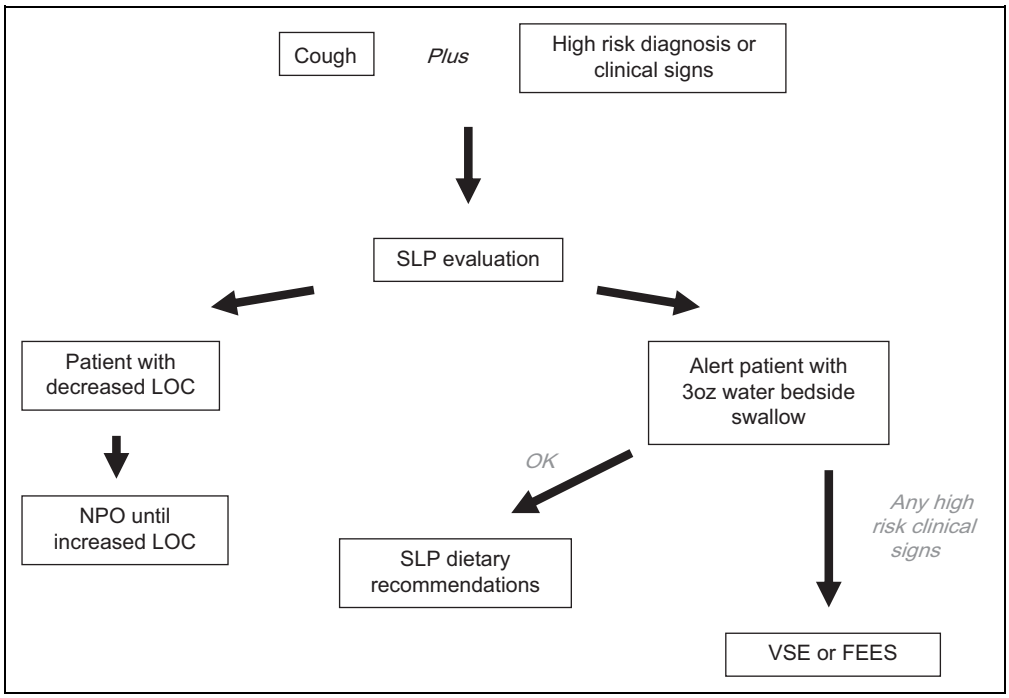

Figure 2. Oral-pharyngeal dysphagia evaluation. SLP **indicates** speech-language pathologist; NPO, nothing by mouth; LOC, level of consciousness; VSE, videofluoroscopic swallow evaluation; FEES, fiberoptic endoscopic evaluation of swallow.

Smith-Hammond and Goldstein have recently reported that objective measurements of voluntary cough can be used to help identify at-risk stroke patients.[17] They examined 96 consecutive patients with stroke with video fluoroscopic swallow evaluation (VSE) or fiber-optic endoscopic evaluation of swallow (FEES), which are generally considered to be the gold standard for assessment of aspiration. Thirty-three of the patients were found to be at risk for aspiration using a penetration-aspiration scale score (PASS) $\geq$5. Objective cough measures were also evaluated in these 96 patients. Three of these objective measures of voluntary cough—expulsive phase rise time (EPRT) >55 m/s, volume acceleration (VA) <50 L/s/s, and expulsive phase peak flow (EPPF) <2.9 L/s—had higher sensitivities (82%, 88%, 91%, respectively) to predict the risk of aspiration than clinical signs such as absent swallow, difficulty handling secretions, or reflexive cough after water bolus. Expulsive phase peak flow and VA measure the rapidity of rise to high flow and high volume cough and both were shown to be independently associated with aspiration as measured by VSE or FEES. Reflexive cough after ice chips or water showed a sensitivity of 39% and specificity of 82%. This indicates that a simple water swallow may miss a significant number of aspirating patients. The authors also noted that 75% of patients that aspirate had cognitive deficits and nearly 90% had speech or language difficulties. Further tightening the cutoffs of cough measures to an EPRT of >67 m/s or a VA of <33 mL/s/s successfully predicted aspirators >90% of the time and >90% of those patients who did not need interventions to reduce their risk for aspiration.[17] Measures of EPRT and VA appear to be promising tools for predicting aspiration risk. These may be superior to simple swallow tests or other clinical parameters.

The 2006 American College of Chest Physicians' (ACCP) evidence-based clinical practice guidelines for diagnosis and management of cough contained a section on cough and aspiration of food and liquids due to oral-pharyngeal dysphagia.[12] There were 15 recommendations overall. Most of these were moderate recommendations (grade B) with a low level of evidence but a substantial net benefit. The guideline panel recommended patients with cough and high risk of aspiration on history and screening should be referred to a speech-language pathologist (SLP) for oral-pharyngeal swallow evaluation. Those patients that are at high risk for aspiration by diagnosis are patients with Alzheimer's disease, cerebrovascular disease, and those that are intubated or ventilated for >48 hours. Patients at high risk have the following clinical signs: malnutrition, dysphonia, weak cough, reflexive cough, drooling, require oral pharyngeal suctioning, or a history of coughing or choking with eating or drinking. They should also have a careful assessment of nutritional needs. Oral feedings should be held in patients with reduced level of consciousness, and a water swallow test performed in alert patients. Video fluoroscopic swallow evaluation or FEES should be used to evaluate swallowing to identify patients with dysphagia so that appropriate treatment can be initiated (Figure 2). Treatment should include the use of an organized multidisciplinary team that includes a physician, a dietician, a speech therapist, a nurse, and physical and occupational therapists. This allows

Table 1. Definitions of Types of Pneumonia and Associated Organisms

Pneumonia Type	Definition	Organisms
Health care associated pneumonia (HCAP)	Pneumonia in a patient closely associated with the health care system: hemodialysis, wound care clinic, recent IV abx, chemotherapy, nursing home, recent hospitalization	Multidrug-resistant organisms (MDR)
		Early (<4 days)
HAP (Hospital associated pneumonia)	Pneumonia in a patient occurring in the hospital >48 hr after admission, not previously incubating	*Enterobacter H influenzae Strep* species Methicillin-sensitive *S aureus* (MSSA)
		Late (>5 days)
Ventilator associated pneumonia (VAP)	Pneumonia in a patient occurring >48-72 hr after intubation	*P aeruginosa, K pneumoniae, E coli, Acinetobacter*, Methicillin-resistant *S aureus* (MRSA)

appropriate compensatory maneuvers, dietary modifications, and surgical interventions to be considered. There is data to suggest a comprehensive multidisciplinary program to assess dysphagia in patients with stroke can reduce the risk of pneumonia.[19] Although the Joint Commission removed the requirement that a swallow screen for dysphagia be performed on all ischemic and hemorrhagic stroke patients before being given food, water, or medication by mouth from their performance measures in January 2010, this remains a part of other stroke quality programs.[20]

Pneumonia After Stroke: Characteristics

Pneumonia in stroke is often from aspiration and therefore will usually affect the dependent portions of the lungs. The superior segments of the lower lobes are actually also posterior, such that aspirated material or secretions would drain there first in the supine patient. This often occurs on the right side more than the left as the right main stem bronchus is more directly aligned with the trachea. However, patients are routinely rotated and repositioned such that any location is possible.

Stroke-related pneumonia is likely a health care–associated or hospital-associated event, as patients are older, often ill or disabled, and part of the health care system. Most hospitalized patients are colonized with hospital flora within 48 hours.[21] Health care–associated pneumonias (HCAP), hospital-associated (HAP), and ventilator-associated pneumonia (VAP) are related, yet somewhat distinct[22] (Table 1). Hospital-associated pneumonia is a pneumonia occurring in the hospital greater than 48 hours after admission that was not previously incubating.[23] Ventilator-associated pneumonia is the term applied to pneumonia occurring more than 48 to 72 hours after intubation. Health care–associated pneumonias is pneumonia in a patient who has been closely associated with the health care system and exposed to its flora (eg, hemodialysis, wound care within last 30 days, recent IV antibiotics, chemotherapy, nursing home, or prior hospitalization for $\geq$2 days in the last 3 months).[24] Hospital-associated pneumonia and VAP are categorized as early or late onset. This distinction is important because late onset HAP or VAP (occurring $\geq$5 days into hospitalization) more often is associated with multidrug resistant pathogens (MDR) than early ($\leq$4 days) HCAP. These important distinctions guide empiric treatment early in the patient's course (prior to culture results). However, if a patient develops early HAP but came in with prior health care–associated risk factors, they should be considered and treated as later onset HAP due to their prior environmental exposures.[24]

Less virulent bacteria and anaerobes that normally inhabit the upper airway and stomach can cause aspiration pneumonia. While pneumococcus or other aerobic bacteria may be present, community-acquired aspiration often involves anaerobes that are more indolent, or may have mixed flora. Anaerobes are difficult to culture and often treatment in this setting is empiric.[25] If there is a suspicion for mixed flora with aerobic organisms, or if the patient has health care–associated aspiration/pneumonia, broader coverage would be required.

Pneumonia After Stroke: Microbiology

Acute post-stroke pneumonia often involves recently hospitalized patients and the microbiology resembles that of HAP, HCAP, or VAP. This often includes aerobic gram-negative bacteria such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Enterobacter*, *Escherichia coli*, and *Acinetobacter*. Methicillin-resistant *Staphylococcus aureus* (MRSA) is becoming more common but other S*taphylococcus* species are still prevalent.[22,26] Early onset HAP is less likely to have MDR bacteria such as *Pseudomonas*, *Acinetobacter*, or MRSA and more likely to have less resistant organisms such as *Enterobacter*, *Haemophilus influenzae*, MSSA, or *Streptococcus* species.[27] The specific pathogen is often identified in only 25% of patients, even on bronchoalveolar lavage (BAL) or tracheal culture.[26] *Candida* species usually represent colonization or tracheal involvement rather than pneumonia, as immunocompetent hosts are rarely afflicted with viral or fungal pneumonia. It is essential to monitor local hospital and community pathogens, especially MDR pathogens; this information can be incorporated into decisions about initial empiric therapy. Timely local surveillance data is critical.[22] Risk

Table 2. Risk Factors for MDR Pathogens[24]

Risk Factors for MDR Pathogens
Antibiotics within previous 90 days
Currently hospitalized 5 or more days
High frequency of antibiotic resistance in hospital
Hospitalized 2 or more days within the previous 90 days
Residence in nursing home
Home infusion therapy
Chronic dialysis
Home wound care
Family member with MDR pathogen
Immunosuppressive disease or therapy

Table 3. Empiric Therapy for Suspected MDR Pathogens[24]

Empiric Therapy for Suspected MDR Pathogens
Antipseudomonal cephalosporin (cefepime, ceftzidime)
Or
Antipseudomonal carbepenem (imipenem, meropenem)
Or
Beta-lactam/beta-lactamase inhibitor (piperacillin-tazobactam)
Plus
Antipseudomonal fluoroquiolone (ciprofloxacin, levofloxacin)
Or
Aminoglycoside (amikacin, gentamycin, tobramycin)
Plus
Linezolid
Or
Vancomycin

factors for MDR infection in HAP, VAP, or HCAP are defined in the 2005 ATS IDSA guidelines (Table 2).

The diagnosis of HAP in any patient is difficult, let alone in neurologically impaired patients with stroke having poor cough and atelectasis. Therapy is often empiric. Lower respiratory tract cultures may be difficult to obtain in nonintubated patients. Blood or pleural cultures are definitive guides if positive, although the sensitivity of blood cultures may be less than 25%.[28] Colonization of the respiratory tract may precede the development of pneumonia and it has been shown that ventilator-associated tracheobronchitis (VAT) may be an important risk factor for subsequent VAP. Preemptive treatment with targeted therapy in this setting may help prevent VAP.[29] Lower respiratory samples should be obtained on all patients, especially patients that are ventilated. These include endotracheal aspirates, bronchoalveolar lavage, or a protected brush specimen. If lower respiratory tract cultures are sterile and there have been no new antibiotics within 24 hours, bacterial pneumonia is extremely rare, although *Legionella* or viral disease would still be a consideration.[22,30]

Pneumonia After Stroke: Treatment

Most patients with stroke and pneumonia will likely have been hospitalized or be considered health care–associated in one way or another. Initial antibiotic selection is often empiric as culture material is not often available. Therefore, the choice of treatment should be determined by the patient's risk of MDR bacteria. The ATS guideline consensus committee 2005 recommendations divide HAP, VAP, or HCAP into early onset (<5 days) and late onset (≥5 days).[22] Early onset disease in patients without other MDR organisms or HCAP risks may be candidates for limited spectrum antibiotic therapy, depending on local pathogens in the community.[22,27] Early onset disease with no prior risks of MDR bacteria (ie, *Streptococcus pneumoniae, Haemophilus influenzae*, MSSA, and antibiotic-sensitive gram negatives) are likely to be covered by ceftriaxone or levofloxacin, moxifloxacin, ciprofloxacin, or ampicillin/sulbactam or ertapenem. Antibiotic recommendations for patients who have clearly aspirated secondary to stroke might reasonably include at least one drug with anaerobic coverage.

The antibiotic recommendations for MDR pathogens reflect the resistance, virulence, and hazards of the usual organisms. Combination therapy is indicated with the antibiotics recommended in the ATS IDSA guidelines (Table 3). There needs to be coverage with two drugs for *Pseudomonas* and other resistant gram negatives (±*Legionella*) and an additional agent for MRSA (vancomycin, linezolid). Because antibiotic pressure on the hospital flora can be considerable, it is important to deescalate therapy and narrow the spectrum if possible.[31] Evaluation of length of treatment has been studied and 8 vs. 15 days of antibiotic therapy for VAP has been shown to be equivalent.[32] Delay in treatment of VAP and HAP may increase mortality[33,34] and timely antibiotics improves outcomes.[35] When there is uncertainty about whether to treat, the CPIS (Clinical Pulmonary Infection Score) scoring system is a useful tool, employing clinical parameters to grade severity and probability of pneumonia.[36]

Linezolid has been shown to be superior to vancomycin in a retrospective analysis of 1019 patients derived from two prior double-blind trials showing equivalency.[37] While it may be preferred based on the combined analysis, there were criticisms of the methods.[38] Linezolid may be preferred if there is renal insufficiency or concerns about adequate levels of vancomycin, especially in communities where the MIC to vancomycin is >2. Linezolid is reported to have higher lung penetration[37] and is likely to be more efficacious if vancomycin levels are suboptimal or the local MIC is higher.

Pneumonia After Stroke: Prevention

We have previously discussed the benefits of early recognition of high-risk patients with a variety of screening methods and the development of a multidisciplinary team focusing on this issue. Interventions to reduce pneumonia risk can then be undertaken by the dysphagia team in patients breathing on their own. Since 6% of ischemic and 30% of hemorrhagic

Table 4. Ventilator Bundle Elements

Ventilator Bundle Elements
Head of bed elevation >30 degrees
Daily "sedative interruption" and assessment of readiness to extubate
PUD prophylaxis
DVT prophylaxis
Daily oral care with chlorhexidine

Abbreviations: PUD, peptic ulcer disease; DVT, deep venous thrombosis.

patients with stroke are intubated,[5] a portion of post-stroke pneumonia risk represents VAP risk.

VAP prevention is part of the 100 k lives campaign (Institute for Health Care Improvement – IHI.org). Guidelines from the Canadian Critical Care Society (2004) and the ATS IDSA (2005) describe the foundations for most of current best evidence-based practice for VAP prevention.[22,39] The intervention proposed by IHI was the use of ventilator ''bundles'' to improve ventilator-care processes. The overall goals are to reduce VAP and VAP-associated morbidity and mortality.[40] The recent emphasis on bundles is driven by the need to improve process reliability,[40] and their successful implementation requires teamwork and a culture of safety.

The IHI ''ventilator bundle'' includes four elements. The Joint Commission measures compliance on five ventilator-bundle elements (Table 4). The remainder of this section will discuss the evidence behind the various methods such as hand washing, shortening ventilator days, patient positioning, and other interventions used to reduce VAP.

Nosocomial infections of all types are reduced by hand washing and have been part of the CDC guidelines for the prevention of nosocomial pneumonia at least since 1985.[41] The importance of hand washing cannot be overestimated (''wash in, wash out'').

The optimal method of reducing VAP is to avoid and shorten ventilator care wherever possible. Noninvasive positive pressure ventilation (NPPV) can be useful in patients with cardiac or pulmonary disease, but perhaps less so in central neurologic disease. Noninvasive positive pressure ventilation studies usually exclude patients with reduced consciousness out of concern for airway protection and aspiration.[42] Some authors consider a GCS <10 to be a contraindication.[43] Much work has been done around reducing ventilator length of stay, primarily focusing on scheduled sedation interruption and use of prescribed daily weaning trials unless otherwise specifically contraindicated.[40,44-46] The correct balance between adequate yet not excessive analgesia and sedation is difficult in neurologically intact patients—more so with the neurologically impaired. Shorter acting agents such as midazolam or propofol for sedation and fentanyl for analgesia are likely to more readily allow frequent assessment of neurologic status.[47] Dexmedetomidine, a centrally acting alpha 2 antagonist does not affect respiratory drive but produces anxiolysis and sedation.[47] Riker et al have recently published a prospective randomized trial of 375 patients comparing midazolam and dexmedetomidine, finding comparable efficacy, but reduced ventilator days and delirium. Dexmedetomidine has not been studied in neurologic units and is currently FDA approved only for <24 hour use.[48]

The use of sedation in neurologically impaired ventilator patients poses unique challenges. Rapid and predictable offset of sedation for intermittent neurological assessment is clinically advantageous generally, but particularly in neurologically impaired individuals. Traditional sedation programs have used hypnotic-based regimens primarily (propofol or midazolam), with addition of an analgesic agent (fentanyl or morphine) secondarily. Karabinis et al report success with an analgesic-based program using remifentanil as the principle sedative. Remifentanil, a very short-acting analgesic agent with organ-independent metabolism was titrated to effect prior to the addition of propofol or midazolam. The study group showed significantly more predictable and rapid awakening in patients with acute brain injury or after neurosurgery than controls.[49] This approach has been shown to be useful in the general critical care population as well.[50]

Girard et al prospectively studies a paired sedation and ventilator weaning protocol (''Wake up and Breathe'').[48] In this study, the intervention group had 3.1 more days breathing without assistance than the control group. The strategy links sedation interruption to the weaning process in a structured fashion.

Many other potentially modifiable risk factors for VAP have been identified and studied. Supine ventilator patients are at greater risk than semi-recumbent patients for VAP[51] and therefore a semi-recumbent goal of 45° has been recommended.[39] In ventilated patients with acute ischemic stroke, some compromise of the head up position may be appropriate in the interests of promoting optimal cerebral perfusion.[52,53] It may also be advisable to withhold tube feedings until a semi-recumbent position is deemed clinically acceptable neurologically, while balancing the risks of aspiration and reflux against the advantages of enteral feeding.

Other interventions to reduce VAP as discussed in the ATS IDSA guidelines include the preferred use of oral intubations to reduce sinusitis and VAP, continuous subglottic suctioning, maintaining adequate staffing levels in ICU, and modulation of oropharyngeal colonization with a scheduled chlorhexidine mouth care program.[22]

Pneumonia After Stroke: Quality Initiatives/Pay for Performance

Pay for performance has come to critical care. Critical care services comprise up to 20% of all hospital costs and >1% of the US GDP.[54-56] Incentives have become more prevalent in an effort to improve outcomes and reduce costs. Many of these incentives will affect patients with stroke both in and out of the ICU, including patients with pneumonia. Medicare will no longer pay an enhanced DRG for some conditions acquired during the inpatient stay, including catheter-associated urinary tract infection, pressure ulcers, falls from bed and vascular

catheter–associated infections.[57] Many neurological patients are at risk for these conditions.

Blue Cross Blue Shield of Michigan has initiated a program wherein documented adherence to each of five elements of the ventilator bundle described previously (Table 4) is a prequalifying requirement to all other hospital pay for performance initiatives. Additionally, the Michigan Hospital Association established the Keystone ICU project, a collaborative regional partnership of nearly 120 ICUs at 76 hospitals focusing on improvements in culture of safety and risk reduction.[58] Specific programs to reduce catheter-related bloodstream infection (CRBSI) and VAP have been implemented statewide with substantial success.[59]

Summary

Stroke affects a significant number of patients every year. There is substantial morbidity and mortality in patients who develop pneumonia after a stroke. Identifying patients at highest risk for developing pneumonia after a stroke should help with treatment and prevention. Highest-associated risks included age >65, dysarthria or no speech due to aphasia, decreased cognition, and dysfunctional swallow. Identifying these patients takes a comprehensive multidisciplinary team. Many of the most effective prevention strategies are those used for prevention of nosocomial pneumonias in general such as hand washing and the use of ventilator bundles. The choice of sedative in ventilated patients may reduce ventilator days and thus the incidence of VAP. The majority of pneumonias associated with stroke are HCAP, HAP, or VAP since some part of the patient's initial diagnosis, treatment, rehabilitation, or permanent residence will involve the health care system. The microbiology of these pneumonias ranges in spectrum from less virulent organisms with less resistance to the more virulent MDR pathogens that plague many hospitals and ICUs these days. Early aggressive broad empiric treatment of non-MDR and MDR pathogens is needed to decrease mortality in post-stroke pneumonia. Quick de-escalation of therapy when cultures are negative and final is equally important in this strategy. Future research should focus on developing better ways of identifying stroke patients at high risk for aspiration and pneumonia and on strategies to prevent this complication.

Declaration of Conflicting Interests

The author(s) declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The author(s) received no financial support for the research and/or authorship of this article.

References

1. Grysiewicz RA, Thomas K, Pandey DK. Epidemiology of ischemic and hemorrhagic stroke: Incidence, prevalence, mortality, and risk factors. *Neurol Clin*. 2008;26(4):871-895, vii.
2. Kung HC, Hoyert DL, Xu J, Murphy SL. Deaths: Final data for 2005. *Natl Vital Stat Rep*. 2008;56(10):1-120.
3. Sellars C, Bowie L, Bagg J, et al. Risk factors for chest infection in acute stroke: A prospective cohort study. *Stroke*. 2007;38(8): 2284-2291.
4. Heuschmann PU, Kolominsky-Rabas PL, Misselwitz B, et al. Predictors of in-hospital mortality and attributable risks of death after ischemic stroke: The German stroke registers study group. *Arch Intern Med*. 2004;164(16):1761-1768.
5. Gujjar AR, Deibert E, Manno EM, Duff S, Diringer MN. Mechanical ventilation for ischemic stroke and intracerebral hemorrhage: Indications, timing, and outcome. *Neurology*. 1998;51(2):447-451.
6. National nosocomial infections surveillance (nnis) system report, data summary from January 1992-april 2000, issued June 2000. *Am J Infect Control*. 2000;28(6):429-448.
7. Warren DK, Shukla SJ, Olsen MA, et al. Outcome and attributable cost of ventilator-associated pneumonia among intensive care unit patients in a suburban medical center. *Crit Care Med*. 2003;31(5):1312-1317.
8. Safdar N, Dezfulian C, Collard HR, Saint S. Clinical and economic consequences of ventilator-associated pneumonia: A systematic review. *Crit Care Med*. 2005;33(10):2184-2193.
9. Scheld WM. Developments in the pathogenesis, diagnosis and treatment of nosocomial pneumonia. *Surg Gynecol Obstet*. 1991;172(1):42-53.
10. Safdar N, Crnich CJ, Maki DG. The pathogenesis of ventilator-associated pneumonia: Its relevance to developing effective strategies for prevention. *Respir Care*. 2005;50(6):725-739; discussion 739-741.
11. Rumbak MJ. The pathogenesis of ventilator-associated pneumonia. *Semin Respir Crit Care Med*. 2002;23(6):427-434.
12. Smith Hammond CA, Goldstein LB. Cough and aspiration of food and liquids due to oral-pharyngeal dysphagia: ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129(1): 154S-168S.
13. Mann G, Hankey GJ, Cameron D. Swallowing function after stroke: Prognosis and prognostic factors at 6 months. *Stroke*. 1999;30(4):744-748.
14. Ding R, Logemann JA. Pneumonia in stroke patients: a retrospective study. *Dysphagia*. 2000;15(2):51-57.
15. Langmore SE, Terpenning MS, Schork A, et al. Predictors of aspiration pneumonia: How important is dysphagia? *Dysphagia*. 1998;13(2):69-81.
16. Hassan A, Khealani BA, Shafqat S, et al. Stroke-associated pneumonia: microbiological data and outcome. *Singapore Med J*. 2006;47(3):204-207.
17. Smith Hammond CA, Goldstein LB, Horner RD, et al. Predicting aspiration in patients with ischemic stroke: Comparison of clinical signs and aerodynamic measures of voluntary cough. *Chest*. 2009;135(3):769-777.
18. McCullough GH, Rosenbek JC, Wertz RT, McCoy S, Mann G, McCullough K. Utility of clinical swallowing examination measures for detecting aspiration post-stroke. *J Speech Lang Hear Res*. 2005;48(6):1280-1293.

19. Doggett DL, Tappe KA, Mitchell MD, Chapell R, Coates V, Turkelson CM. Prevention of pneumonia in elderly stroke patients by systematic diagnosis and treatment of dysphagia: An evidence-based comprehensive analysis of the literature. *Dysphagia*. 2001;16(4):279-295.
20. Summers D, Leonard A, Wentworth D, et al. Comprehensive overview of nursing and interdisciplinary care of the acute ischemic stroke patient: A scientific statement from the American heart association. *Stroke*. 2009;40(8):2911-2944.
21. Garrouste-Orgeas M, Chevret S, Arlet G, et al. Oropharyngeal or gastric colonization and nosocomial pneumonia in adult intensive care unit patients. A prospective study based on genomic DNA analysis. *Am J Respir Crit Care Med*. 1997;156(5):1647-1655.
22. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med*. 2005;171(4):388-416.
23. Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R. Guidelines for preventing health-care–associated pneumonia, 2003: Recommendations of CDC and the healthcare infection control practices advisory committee. *MMWR Recomm Rep*. 2004; 53(3):1-36.
24. Hospital-acquired pneumonia in adults: Diagnosis, assessment of severity, initial antimicrobial therapy, and preventive strategies. A consensus statement, American thoracic society, November 1995. *Am J Respir Crit Care Med*. 1996;153(5):1711-1725.
25. Bartlett JG. Anaerobic bacterial infections of the lung and pleural space. *Clin Infect Dis*. 1993;16(4):S248-S255.
26. Kollef MH, Shorr A, Tabak YP, Gupta V, Liu LZ, Johannes RS. Epidemiology and outcomes of health-care-associated pneumonia: Results from a large us database of culture-positive pneumonia. *Chest*. 2005;128(6):3854-3862.
27. Trouillet JL, Chastre J, Vuagnat A, et al. Ventilator-associated pneumonia caused by potentially drug-resistant bacteria. *Am J Respir Crit Care Med*. 1998;157(2):531-539.
28. Luna CM, Videla A, Mattera J, et al. Blood cultures have limited value in predicting severity of illness and as a diagnostic tool in ventilator-associated pneumonia. *Chest*. 1999;116(4):1075-1084.
29. Craven DE, Chroneou A, Zias N, Hjalmarson KI. Ventilator-associated tracheobronchitis: The impact of targeted antibiotic therapy on patient outcomes. *Chest*. 2009;135(2):521-528.
30. Fagon JY, Chastre J, Wolff M, et al. Invasive and noninvasive strategies for management of suspected ventilator-associated pneumonia. A randomized trial. *Ann Intern Med*. 2000;132(8): 621-630.
31. Micek ST, Ward S, Fraser VJ, Kollef MH. A randomized controlled trial of an antibiotic discontinuation policy for clinically suspected ventilator-associated pneumonia. *Chest*. 2004;125(5): 1791-1799.
32. Chastre J, Wolff M, Fagon JY, et al. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: A randomized trial. *JAMA*. 2003;290(19):2588-2598.
33. Iregui M, Ward S, Sherman G, Fraser VJ, Kollef MH. Clinical importance of delays in the initiation of appropriate antibiotic treatment for ventilator-associated pneumonia. *Chest*. 2002; 122(1):262-268.
34. Kollef MH, Sherman G, Ward S, Fraser VJ. Inadequate antimicrobial treatment of infections: A risk factor for hospital mortality among critically ill patients. *Chest*. 1999;115(2):462-474.
35. Luna CM, Vujacich P, Niederman MS, et al. Impact of bal data on the therapy and outcome of ventilator-associated pneumonia. *Chest*. 1997;111(3):676-685.
36. Singh N, Rogers P, Atwood CW, Wagener MM, Yu VL. Short-course empiric antibiotic therapy for patients with pulmonary infiltrates in the intensive care unit. A proposed solution for indiscriminate antibiotic prescription. *Am J Respir Crit Care Med*. 2000;162(2):505-511.
37. Wunderink RG, Rello J, Cammarata SK, Croos-Dabrera RV, Kollef MH. Linezolid vs vancomycin: Analysis of two double-blind studies of patients with methicillin-resistant staphylococcus aureus nosocomial pneumonia. *Chest*. 2003;124(5):1789-1797.
38. Powers JH, Ross DB, Lin D, Soreth J. Linezolid and vancomycin for methicillin-resistant staphylococcus aureus nosocomial pneumonia: The subtleties of subgroup analyses. *Chest*. 2004; 126(1):314-315, author reply 315-316.
39. Dodek P, Keenan S, Cook D, et al. Evidence-based clinical practice guideline for the prevention of ventilator-associated pneumonia. *Ann Intern Med*. 2004;141(4):305-313.
40. Resar R, Pronovost P, Haraden C, Simmonds T, Rainey T, Nolan T. Using a bundle approach to improve ventilator care processes and reduce ventilator-associated pneumonia. *Jt Comm J Qual Patient Saf*. 2005;31(5):243-248.
41. Boyce JM, White RL, Spruill EY, Wall M. Cost-effective application of the centers for disease control guideline for prevention of nosocomial pneumonia. *Am J Infect Control*. 1985;13(5): 228-232.
42. Yeow ME, Santanilla JI. Noninvasive positive pressure ventilation in the emergency department. *Emerg Med Clin North Am*. 2008;26(4):835-847, x.
43. International consensus conferences in intensive care medicine: Noninvasive positive pressure ventilation in acute respiratory failure. *Am J Respir Crit Care Med*. 2001;163(1):283-291.
44. Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med*. 2000;342(20): 1471-1477.
45. Marelich GP, Murin S, Battistella F, Inciardi J, Vierra T, Roby M. Protocol weaning of mechanical ventilation in medical and surgical patients by respiratory care practitioners and nurses: effect on weaning time and incidence of ventilator-associated pneumonia. *Chest*. 2000;118(2):459-467.
46. Quenot JP, Ladoire S, Devoucoux F, et al. Effect of a nurse-implemented sedation protocol on the incidence of ventilator-associated pneumonia. *Crit Care Med*. 2007;35(9):2031-2036.
47. Brush DR, Kress JP. Sedation and analgesia for the mechanically ventilated patient. *Clin Chest Med*. 2009;30(1):131-141, ix.
48. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (awakening and breathing controlled trial): a randomised controlled trial. *Lancet*. 2008; 371(9607):126-134.

49. Karabinis A, Mandragos K, Stergiopoulos S, et al. Safety and efficacy of analgesia-based sedation with remifentanil versus standard hypnotic-based regimens in intensive care unit patients with brain injuries: A randomised, controlled trial [isrctn50308308]. *Crit Care*. 2004;8(4):R268-R280.
50. Breen D, Karabinis A, Malbrain M, et al. Decreased duration of mechanical ventilation when comparing analgesia-based sedation using remifentanil with standard hypnotic-based sedation for up to 10 days in intensive care unit patients: a randomised trial [isrctn47583497]. *Crit Care*. 2005;9(2):R200-210.
51. Drakulovic MB, Torres A, Bauer TT, Nicolas JM, Nogue S, Ferrer M. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. *Lancet*. 1999;354(9193):1851-1858.
52. Caplan LR, Sergay S. Positional cerebral ischaemia. *J Neurol Neurosurg Psychiatry*. 1976;39(4):385-391.
53. Toole JF. Effects of change of head, limb and body position on cephalic circulation. *N Engl J Med*. 1968;279(6):307-311.
54. Khanduja K, Scales DC, Adhikari NK. Pay for performance in the intensive care unit–opportunity or threat? *Crit Care Med*. 2009;37(3):852-858.
55. Adam S, Odell M. An acute problem? A report of the national confidential enquiry into patient outcome and death. *Nurs Crit Care*. 2005;10(5):225-227.
56. Halpern NA, Bettes L, Greenstein R. Federal and nationwide intensive care units and healthcare costs: 1986-1992. *Crit Care Med*. 1994;22(12):2001-2007.
57. Rosenthal MB. Nonpayment for performance? Medicare's new reimbursement rule. *N Engl J Med*. 2007; 357(16): 1573-1575.
58. Pronovost PJ, Berenholtz SM, Goeschel C, et al. Improving patient safety in intensive care units in michigan. *J Crit Care*. 2008;23(2):207-221.
59. Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med*. 2006;355(26):2725-2732.